ACC.14
TCT@ACC-i2 | innovation in intervention

A1954
JACC April 1, 2014
Volume 63, Issue 12

Valvular Heart Disease

EVALUATION OF FAMILIAL CLUSTERING OF CARDIAC VALVE DISEASES TO EMPOWER GENETIC STUDIES OF HIGH-RISK PEDIGREES

Poster Contributions
Hall C
Saturday, March 29, 2014, 10:00 a.m.-10:45 a.m.

Session Title: Valvular Heart Disease: Pathophysiology, Outcome & Risk
Abstract Category: 28. Valvular Heart Disease: Clinical
Presentation Number: 1122-348

Authors: *Benjamin Davies Horne, Stephen Clayson, John Doty, Joseph B. Muhlestein, John Carlquist, Jeffrey L. Anderson, Stacey Knight, Intermountain Medical Center, Salt Lake City, UT, USA, University of Utah, Salt Lake City, UT, USA*

Background: Previously we showed that death due to aortic valve disease and due to mitral valve disease aggregate within families in the Utah Population Database. While individual genetic loci for mitral valve prolapse and familiality of bicuspid aortic valve have been reported, systematic investigation of these and other cardiac valve conditions has not occurred. To better identify genetic contributions to the multiple common cardiac valve phenotypes, this study utilized the Intermountain Genealogical Registry (IGR) to study the familial clustering of clinical diagnoses of cardiac valve diseases.

Methods: IGR contains the genealogies of more than 23 million individuals, including more than 700,000 patients seen at Intermountain Healthcare during the last 20 years and their ancestors. A genealogical index of familiality (GIF), a measure of the average pairwise kinship of coefficient, was calculated for cardiac valve disease phenotypes (defined by ICD-9 codes). Empirical p-values were computed using sets of age- and sex-matched controls.

Results: The GIF was significantly higher than controls for all aortic and mitral valve diseases (GIF=0.476, n=6057 cases, p<0.001), all aortic valve disease (ICD-9 395.x & 424.1, GIF=0.479, n=2736 cases, p=0.026), aortic disease not specified as stenosis (395.1 & 424.1, GIF=0.468, n=2708 cases, p=0.025), all mitral valve disease (394.x & 424.0, GIF=0.476, n=3476 cases, p=0.003), and mitral valve disorder (394.1 & 424.0, GIF=0.467, n=3330 cases, p<0.001). When congenital cases of aortic valve disease were excluded (ICD-9 424.1 excluding 746.4, n=2635 cases), the significance increased with GIF=0.479 (p=0.004), with the most common exclusion being bicuspid aortic valve cases. For aortic insufficiency (395.1, n=55 cases), GIF was exceptionally high (GIF=0.985) but the small sample size resulted in a trend (p=0.06).

Conclusions: Diagnoses of aortic valve disease and mitral valve disease were found to cluster within families, expanding on prior findings and suggesting that high-risk families may be identified. Further studies should evaluate genetic sequence variants in these patients and their families to discover loci for cardiac valve disorders.